

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1. (Canceled)
2. (Allowed) A procytotoxin comprising a peptide comprising at least one lysine residue bound via a peptide bond to at least one amino acid via the ϵ -amino group of said lysine residue, wherein said peptide without said modification is a cytotoxic peptide, and wherein said at least one amino acid bound via the ϵ -amino group of said lysine residue acts to prevent the peptide from forming a lytically active conformation, and wherein the cytotoxic peptide is a pore-forming cytolytic peptide.
3. (Allowed) The procytotoxin of claim 2, wherein the pore-forming cytolytic peptide is selected from the group consisting of Ae I, cytolysin of sea anemone, aerolysin, amatoxin, amoebapore, amoebapore homolog from *Entamoeba dispar*, brevinin-1E, brevinin-2E, barbatolysin, cytolysin of *Enterococcus faecalis*, delta hemolysin, diphtheria toxin, El Tor cytolysin of *Vibrio cholerae*, equinatoxin, enterotoxin of *Aeromonas hydrophila*, esculentin, granulysin, haemolysin of *Vibrio parahaemolyticus*, intermedilysin of *Streptococcus intermedius*, the lentivirus lytic peptide, leukotoxin of *Actinobacillus actinomycetemcomitans*, magainin, melittin, membrane-associated lymphotoxin, Met-enkephalin, neokyotorphin, neokyotorphin fragment 1, neokyotorphin fragment 2, neokyotorphin fragment 3, neokyotorphin fragment 4, NK-lysin, paradaxin, perforin, perfringolysin O, theta-toxin, of *Clostridium perfringens*, phallolysin, phallotoxin, and streptolysin, ~~analogs of the pore-forming cytolytic peptide, and derivatives of the pore-forming cytolytic peptide.~~
4. (Currently Amended) The procytotoxin of claim 3, wherein the cytolytic peptide is an amoebapore[I.I]

5. (Allowed) The procytotoxin of claim 4, comprising the following structure: Gly-Phe-Ile-Ala-Thr-Leu-Cys-Thr-Lys(R)-Val-Leu-Asp-Phe-Gly-Ile-Asp-Lys(R)-Leu-Ile-Gln-Leu-Ile-Glu-Asp-Lys(R) (SEQ ID NO: 1), wherein at least one (R) is independently selected from the group consisting of $[\epsilon\text{-}\gamma]\text{-Glu}$, $[\epsilon\text{-}\gamma]\text{-Glu-}[\alpha\text{-}\gamma]\text{-(Glu)}_{1-3}$, $[\epsilon\text{-}\alpha]\text{-(Phe)}_{1-3}$, $[\epsilon\text{-}\alpha]\text{-(Tyr)}_{1-3}$, $[\epsilon\text{-}\alpha]\text{-(Trp)}_{1-3}$, $[\epsilon\text{-}\alpha]\text{-(Lys)}_{1-3}$ and $[\epsilon\text{-}\alpha]\text{-(Arg)}_{1-3}$, wherein $[\epsilon\text{-}\gamma]$ represents a peptide bond between the epsilon amino group of lysine and the gamma carboxyl group of the adjacent glutamate, $[\alpha\text{-}\gamma]$ represents a peptide bond between the alpha amino group of the first glutamate and the gamma carboxyl group of the second glutamate, $[\epsilon\text{-}\alpha]$ represents a peptide bond between the epsilon amino acid of lysine and the alpha carboxyl group of the indicated amino acid and the subscript indicates that additional numbers of the designated amino acid can be linked to the first via conventional peptide bonds.

6. (Allowed) The procytotoxin of claim 3, wherein the cytolytic peptide is a melittin.

7. (Allowed) The procytotoxin of claim 6 consisting essentially of the following structure: Gly-Ile-Gly-Ala-Val-Leu-Lys(R)-Val-Leu-Thr-Thr-Gly-Leu-Pro-Ala-Leu-Ile-Ser-Trp-Ile-Lys(R)-Arg-Lys(R)-Arg-Gln-Gln (SEQ ID NO: 2), wherein at least one (R) is independently selected from the group consisting of $[\epsilon\text{-}\gamma]\text{-Glu}$, $[\epsilon\text{-}\gamma]\text{-Glu-}[\alpha\text{-}\gamma]\text{-(Glu)}_{1-3}$, $[\epsilon\text{-}\alpha]\text{-(Phe)}_{1-3}$, $[\epsilon\text{-}\alpha]\text{-(Tyr)}_{1-3}$, $[\epsilon\text{-}\alpha]\text{-(Trp)}_{1-3}$, $[\epsilon\text{-}\alpha]\text{-(Lys)}_{1-3}$ and $[\epsilon\text{-}\alpha]\text{-(Arg)}_{1-3}$, wherein $[\epsilon\text{-}\gamma]$ represents a peptide bond between the epsilon amino group of lysine and the gamma carboxyl group of the adjacent glutamate, $[\alpha\text{-}\gamma]$ represents a peptide bond between the alpha amino group of the first glutamate and the gamma carboxyl group of the second glutamate, $[\epsilon\text{-}\alpha]$ represents a peptide bond between the epsilon amino group of lysine and the alpha carboxyl group of the indicated amino acid and the subscript indicates that additional numbers of the designated amino acid can be linked to the first via conventional peptide bonds.

8. (Currently Amended) A procytotoxin comprising a peptide comprising at least one lysine residue bound via a peptide bond to at least one amino acid via the ϵ -amino group of said lysine residue, wherein said peptide without said modification is a cytotoxic peptide, and wherein said at least one amino acid bound via the ϵ -amino group of said lysine residue

acts to prevent the peptide from forming a lytically active conformation, and wherein said procytotoxin comprises a structure selected from the group consisting of: ~~N-Gly-Phe-Ile-Ala-Thr-Leu-Cys-Thr-Lys-Val-Leu-Asp-Phe-Gly-Ile-Asp-Lys-Leu-Ile-Gln-Leu-Ile-Glu-Asp-Lys([ε-g]-Glu-[α-g]-Glu)-CONH₂-N-Gly-Phe-Ile-Ala-Thr-Leu-Cys-Thr-Lys-Val-Leu-Asp-Phe-Gly-Ile-Asp-Lys-Leu-Ile-Gln-Leu-Ile-Glu-Asp-Lys([ε-γ]-Glu-[α-γ]-Glu)-CONH₂~~ (SEQ ID NO: 8) and ~~NH₂-Gly-Ile-Gly-Ala-Val-Leu-Lys-Val-Leu-Thr-Thr-Gly-Leu-Pro-Ala-Leu-Ile-Ser-Trp-Ile-Lys([ε-g]-Glu-[α-g]-Glu)-Arg-Lys([ε-g]-Glu-[α-g]-Glu)-Arg-Gln-Gln-COOH~~ NH₂-Gly-Ile-Gly-Ala-Val-Leu-Lys-Val-Leu-Thr-Thr-Gly-Leu-Pro-Ala-Leu-Ile-Ser-Trp-Ile-Lys([ε-γ]-Glu-[α-γ]-Glu)-Arg-Lys([ε-γ]-Glu-[α-γ]-Glu)-Arg-Gln-Gln-COOH (SEQ ID NO: 12).

9. (Allowed) A pharmaceutical composition, comprising the procytotoxin of claim 2, and a pharmaceutically acceptable excipient.

10. (Canceled)

11. (Canceled)

12. (Currently Amended) The method of claim 13 [[,]] wherein said cancer cell is selected from the group consisting of prostate, ovarian, lung and skin cells.

13. (Allowed) A method for selectively destroying a target cell that is a cancer cell, comprising contacting the target cell with a procytotoxin, which comprises a peptide comprising at least one lysine residue bound via a peptide bond to at least one amino acid via the ε-amino group of said lysine residue, wherein said peptide without said modification is a cytotoxic peptide, and wherein said at least one amino acid bound via the ε-amino group of said lysine residue acts to prevent the peptide from forming a lytically active conformation, and wherein the cytotoxic peptide is a pore-forming cytolytic peptide.

14. (Allowed) The method of claim 13, wherein the pore-forming cytolytic peptide is selected from the group consisting of Ae I, cytolysin of sea anemone, aerolysin, amatoxin, amoebapore, amoebapore homolog from *Entamoeba dispar*, brevinin-1E, brevinin-2E, barbatolysin, cytolysin of *Enterococcus faecalis*, delta hemolysin, diphtheria toxin, El Tor

cytolysin of *Vibrio cholerae*, equinatoxin, enterotoxin of *Aeromonas hydrophila*, esculentin, granulysin, haemolysin of *Vibrio parahaemolyticus*, intermedilysin of *Streptococcus intermedius*, the lentivirus lytic peptide, leukotoxin of *Actinobacillus actinomycetemcomitans*, magainin, melittin, membrane-associated lymphotoxin, Met-enkephalin, neokyotorphin, neokyotorphin fragment 1, neokyotorphin fragment 2, neokyotorphin fragment 3, neokyotorphin fragment 4, NK-lysin, paradaxin, perforin, perfringolysin O, theta-toxin, of *Clostridium perfringens*, phallolysin, phallotoxin, and streptolysin.

15. (Allowed) The method of claim 14, wherein the cytolytic peptide is an amoebapore.

16. (Currently Amended) The method of claim 14, wherein the procytotoxin comprises the following structure: Gly-Phe-Ile-Ala-Thr-Leu-Cys-Thr-Lys(R)-Val-Leu-Asp-Phe-Gly-Ile-Asp-Lys(R)-Leu-Ile-Gln-Leu-Ile-Glu-Asp-Lys(R) (SEQ ID NO: 1), wherein at least one (R) is independently selected from the group consisting of ~~{e-g}-Glu, {e-g}-Glu-{a-g}-(Glu)₁₋₃, {e-a}-(Phe)₁₋₃, {e-a}-(Tyr)₁₋₃, {e-a}-(Trp)₁₋₃, {e-a}-(Lys)₁₋₃ and {e-a}-(Arg)₁₋₃~~ [ε-γ]-Glu, [ε-γ]-Glu-[α-γ]-(Glu)₁₋₃, [ε-α]-(Phe)₁₋₃, [ε-α]-(Tyr)₁₋₃, [ε-α]-(Trp)₁₋₃, [ε-α]-(Lys)₁₋₃ and [ε-α]-(Arg)₁₋₃, wherein ~~{e-g}~~ [ε-γ] represents a peptide bond between the epsilon amino group of lysine and the gamma carboxyl group of the adjacent glutamate, ~~{a-g}~~ [α-γ] represents a peptide bond between the alpha amino group of the first glutamate and the gamma carboxyl group of the second glutamate, ~~{e-a}~~ [ε-α] represents a peptide bond between the epsilon amino acid of lysine and the alpha carboxyl group of the indicated amino acid and the subscript indicates that additional numbers of the designated amino acid can be linked to the first via conventional peptide bonds.

17. (Allowed) The method of claim 14, wherein the cytolytic peptide is a melittin.

18. (Currently Amended) The method of claim 17, wherein the procytotoxin consists essentially of the following structure: Gly- Ile-Gly-Ala-Val-Leu-Lys(R)-Val-Leu-Thr-Thr-Gly-Leu-Pro-Ala-Leu-Ile-Ser-Trp-Ile-Lys(R)-Arg-Lys(R)-Arg-Gln-Gln (SEQ ID NO: 2), wherein at least one (R) is independently selected from the group consisting of ~~{e-g}~~-

~~Glu, [e-g]-Glu-[a-g]-(Glu)₁₋₃, [e-a]-(Phe)₁₋₃, [e-a]-(Tyr)₁₋₃, [e-a]-(Trp)₁₋₃, [e-a]-(Lys)₁₋₃ and [e-a]-(Arg)₁₋₃-[ε-γ]-Glu, [ε-γ]-Glu-[α-γ]-(Glu)₁₋₃, [ε-α]-(Phe)₁₋₃, [ε-α]-(Tyr)₁₋₃, [ε-α]-(Trp)₁₋₃, [ε-α]-(Lys)₁₋₃ and [ε-α]-(Arg)₁₋₃~~, wherein ~~[e-g]-[ε-γ]~~ represents a peptide bond between the epsilon amino group of lysine and the gamma carboxyl group of the adjacent glutamate, ~~[a-g]~~ ~~[α-γ]~~ represents a peptide bond between the alpha amino group of the first glutamate and the gamma carboxyl group of the second glutamate, ~~[e-a]~~ ~~[ε-α]~~ represents a peptide bond between the epsilon amino group of lysine and the alpha carboxyl group of the indicated amino acid and the subscript indicates that additional numbers of the designated amino acid can be linked to the first via conventional peptide bonds.

19. (Currently Amended) A method for selectively destroying a target cell that is a cancer cell, comprising contacting the target cell with a procytotoxin, which comprises a peptide comprising at least one lysine residue bound via a peptide bond to at least one amino acid via the ε-amino group of said lysine residue, wherein said peptide without said modification is a cytotoxic peptide, and wherein said at least one amino acid bound via the ε-amino group of said lysine residue acts to prevent the peptide from forming a lytically active conformation, and the procytotoxin comprises the structure ~~NH₂-Gly-Ile-Gly-Ala-Val-Leu-Lys-Val-Leu-Thr-Thr-Gly-Leu-Pro-Ala-Leu-Ile-Ser-Trp-Ile-Lys([e-g]-Glu-[a-g]-Glu)-Arg-Lys([e-g]-Glu-[a-g]-Glu)-Arg-Gln-Gln-COOH~~ NH₂-Gly-Ile-Gly-Ala-Val-Leu-Lys-Val-Leu-Thr-Thr-Gly-Leu-Pro-Ala-Leu-Ile-Ser-Trp-Ile-Lys([ε-γ]-Glu-[α-γ]-Glu)-Arg-Lys([ε-γ]-Glu-[α-γ]-Glu)-Arg-Gln-Gln-COOH (SEQ ID NO: 12).

20. (Allowed) The procytotoxin of claim 2, wherein the pore-forming cytolytic peptide is selected from the group consisting of Ae I, cytolsin of sea anemone, aerolysin, amatoxin, amoebapore, amoebapore homolog from *Entamoeba dispar*, brevinin-1E, brevinin-2E, barbatolysin, cytolsin of *Enterococcus faecalis*, delta hemolysin, diphtheria toxin, El Tor cytolsin of *Vibrio cholerae*, equinatoxin, enterotoxin of *Aeromonas hydrophila*, esculentin, granulysin, haemolysin of *Vibrio parahaemolyticus*, intermedilysin of *Streptococcus intermedius*, the lentivirus lytic peptide, leukotoxin of *Actinobacillus actinomycetemcomitans*, magainin, melittin, membrane-associated lymphotoxin, Met-enkephalin, neokytorphin, neokytorphin fragment 1, neokytorphin fragment 2,

neokytorphin fragment 3, neokytorphin fragment 4, NK-lysin, paradaxin, perforin, perfringolysin O, theta-toxin, of *Clostridium perfringens*, phallolysin, phalloxin, and streptolysin.

21. (Allowed) The procytotoxin of claim 20, wherein the cytolytic peptide is an amoebapore.

22. (Allowed) The procytotoxin of claim 21, comprising the following structure: Gly-Phe-Ile-Ala-Thr-Leu-Cys-Thr-Lys(R)-Val-Leu-Asp-Phe-Gly-Ile-Asp-Lys(R)-Leu-Ile-Gln-Leu-Ile-Glu-Asp-Lys(R) (SEQ ID NO. 1), wherein at least one (R) is independently selected from the group consisting of $[\epsilon-\gamma]$ -Glu, $[\epsilon-\gamma]$ -Glu- $[\alpha-\gamma]$ -(Glu)₁₋₃, $[\epsilon-\alpha]$ -(Phe)₁₋₃, $[\epsilon-\alpha]$ -(Tyr)₁₋₃, $[\epsilon-\alpha]$ -(Trp)₁₋₃, $[\epsilon-\alpha]$ -(Lys)₁₋₃ and $[\epsilon-\alpha]$ -(Arg)₁₋₃, wherein:

$[\epsilon-\gamma]$ represents a peptide bond between the epsilon amino group of lysine and the gamma carboxyl group of the adjacent glutamate,

$[\alpha-\gamma]$ represents a peptide bond between the alpha amino group of the first glutamate and the gamma carboxyl group of the second glutamate,

$[\epsilon-\alpha]$ represents a peptide bond between the epsilon amino acid of lysine and the alpha carboxyl group of the indicated amino acid, and

the subscript indicates that additional numbers of the designated amino acid can be linked to the first via conventional peptide bonds.

23. (Allowed) The procytotoxin of claim 22, wherein R is independently selected from the group consisting of $[\epsilon-\gamma]$ -Glu and $[\epsilon-\gamma]$ -Glu- $[\alpha-\gamma]$ -(Glu)₁₋₃, wherein:

$[\epsilon-\gamma]$ represents a peptide bond between the epsilon amino group of lysine and the gamma carboxyl group of the adjacent glutamate,

$[\alpha-\gamma]$ represents a peptide bond between the alpha amino group of the first glutamate and the gamma carboxyl group of the second glutamate, and

the subscript indicates that additional numbers of the designated amino acid can be linked to the first via conventional peptide bonds.

24. (Allowed) A method for selectively destroying a target cell that is a cancer cell, comprising contacting the target cell with a procytotoxin, which comprises a peptide

comprising at least one lysine residue bound via a peptide bond to at least one amino acid via the ϵ -amino group of said lysine residue, wherein said peptide without said modification is a cytotoxic peptide, and wherein said at least one amino acid bound via the ϵ -amino group of said lysine residue acts to prevent the peptide from forming a lytically active conformation, and the procytotoxin comprises the structure N-Gly-Phe-Ile-Ala-Thr-Leu-Cys-Thr-Lys-Val-Leu-Asp-Phe-Gly-Ile-Asp-Lys-Leu-Ile-Gln-Leu-Ile-Glu-Asp-Lys($[\epsilon\text{-}\gamma]$ -Glu- $[\alpha\text{-}\gamma]$ -Glu)-CONH₂ (SEQ ID NO. 8).

25. (Allowed) A procytotoxin comprising a peptide comprising at least one lysine residue bound via a peptide bond to at least one amino acid via the ϵ -amino group of said lysine residue,

(i) wherein said peptide without the modification is a pore-forming cytolytic peptide,

(ii) wherein said at least one amino acid bound via the ϵ -amino group of said lysine residue acts to prevent the peptide from forming a lytically active conformation, and

(iii) wherein said cytolytic peptide need not be internalized to cause target-specific cell death.

26. (Allowed) The procytotoxin of claim 25, wherein the pore-forming cytolytic peptide is selected from the group consisting of amoebapore and melittin.